



SEQUENCE LISTING

<110> Rose, David
Kuntz, Douglas
Van Den Elsen, Jean

<120> MANNOSIDASE STRUCTURES

<130> 12243.19USU1

<140> US 09/960,226
<141> 2001-09-21

<150> US 60/263,458
<151> 2001-01-23

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<170> PatentIn version 3.1

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ctc ggg aga tct agc cac cat cat cat cac gga gaa ttc gac gat 96
Leu Gly Arg Ser Ser His His His His His Gly Glu Phe Asp Asp
20 25 30

cca ata aga cct cca ctt aaa gtg gct cgt tcc ccg agg cca ggg caa 144
Pro Ile Arg Pro Pro Leu Lys Val Ala Arg Ser Pro Arg Pro Gly Gln
35 40 45

tgc caa gat gtg gtc caa gac gtg ccc aat gtg gat gta cag atg ctg 192
Cys Gln Asp Val Val Gln Asp Val Pro Asn Val Asp Val Gln Met Leu
50 55 60

gag cta tac gat cgc atg tcc ttc aag gac ata gat gga ggc gtg tgg 240
Glu Leu Tyr Asp Arg Met Ser Phe Lys Asp Ile Asp Gly Gly Val Trp
65 70 75 80

aaa cag ggc tgg aac att aag tac gat cca ctg aag tac aac gcc cat 288
Lys Gln Gly Trp Asn Ile Lys Tyr Asp Pro Leu Lys Tyr Asn Ala His
85 90 95

cac aaa cta aaa gtc ttc gtt gtg ccg cac tcg cac aac gat cct gga

336

His	Lys	Leu	Lys	Val	Phe	Val	Val	Pro	His	Ser	His	Asn	Asp	Pro	Gly			
100								105							110			
tgg	att	cag	acg	ttt	gag	gaa	tac	tac	cag	cac	gac	acc	aag	cac	atc		384	
Trp	Ile	Gln	Thr	Phe	Glu	Glu	Tyr	Tyr	Gln	His	Asp	Thr	Lys	His	Ile			
115								120							125			
ctg	tcc	aat	gca	cta	cg	cat	ctg	cac	gac	aat	ccc	gag	atg	aag	ttc		432	
Leu	Ser	Asn	Ala	Leu	Arg	His	Leu	His	Asp	Asn	Pro	Glu	Met	Lys	Phe			
130							135								140			
atc	tgg	g	g	g	a	a	tcc	tac	ttt	gct	cg	ttc	tat	cac	gat	ttg	gga	480
Ile	Trp	Ala	Glu	Ile	Ser	Tyr	Phe	Ala	Arg	Phe	Tyr	His	Asp	Leu	Gly			
145							150				155				160			
gag	aac	aaa	aag	ctg	cag	atg	aag	tcc	att	gta	aag	aat	gga	cag	ttg		528	
Glu	Asn	Lys	Lys	Leu	Gln	Met	Lys	Ser	Ile	Val	Lys	Asn	Gly	Gln	Leu			
165							170				175							
gaa	ttg	gaa	ttt	gtg	act	gga	gga	tgg	gta	atg	ccg	gac	gag	gcc	aac		576	
Glu	Leu	Glu	Phe	Val	Thr	Gly	Gly	Trp	Val	Met	Pro	Asp	Glu	Ala	Asn			
180							185				190							
tcc	cac	tgg	cga	aac	gta	ctg	ctg	cag	ctg	acc	gaa	ggg	caa	aca	tgg		624	
Ser	His	Trp	Arg	Asn	Val	Leu	Leu	Gln	Leu	Thr	Glu	Gly	Gln	Thr	Trp			
195							200				205							
ttg	aag	caa	tcc	atg	aat	gtc	aca	ccc	act	gct	tcc	tgg	gcc	atc	gat		672	
Leu	Lys	Gln	Phe	Met	Asn	Val	Thr	Pro	Thr	Ala	Ser	Trp	Ala	Ile	Asp			
210							215				220							
ccc	ttc	gga	cac	agt	ccc	act	atg	ccg	tac	att	ttg	cag	aag	agt	gg		720	
Pro	Phe	Gly	His	Ser	Pro	Thr	Met	Pro	Tyr	Ile	Leu	Gln	Lys	Ser	Gly			
225							230				235				240			
ttc	aag	aat	atg	ctt	atc	caa	agg	acg	cac	tat	tcg	gtt	aag	aag	gaa		768	
Phe	Lys	Asn	Met	Leu	Ile	Gln	Arg	Thr	His	Tyr	Ser	Val	Lys	Lys	Glu			
245							250				255							
ctg	gcc	caa	cag	cga	cag	ctt	gag	ttc	ctg	tgg	cgc	cag	atc	tgg	gac		816	
Leu	Ala	Gln	Gln	Arg	Gln	Leu	Glu	Phe	Leu	Trp	Arg	Gln	Ile	Trp	Asp			
260							265				270							
aac	aaa	ggg	gac	aca	gct	ctc	ttc	acc	cac	atg	atg	ccc	ttc	tac	tcg		864	
Asn	Lys	Gly	Asp	Thr	Ala	Leu	Phe	Thr	His	Met	Met	Pro	Phe	Tyr	Ser			
275							280				285							
tac	gac	att	cct	cat	acc	tgt	.ggt	cca	gat	ccc	aag	gtt	tgc	tgt	cag		912	
Tyr	Asp	Ile	Pro	His	Thr	Cys	Gly	Pro	Asp	Pro	Lys	Val	Cys	Cys	Gln			
290							295				300							
ttc	gat	ttc	aaa	cga	atg	ggc	tcc	ttc	ggt	ttg	agt	tgt	cca	tgg	aag		960	
Phe	Asp	Phe	Lys	Arg	Met	Gly	Ser	Phe	Gly	Leu	Ser	Cys	Pro	Trp	Lys			
305							310				315				320			
gtg	ccg	ccg	cgt	aca	atc	agt	gat	caa	aat	gtg	gca	gca	cgc	tca	gat		1008	
Val	Pro	Pro	Arg	Thr	Ile	Ser	Asp	Gln	Asn	Val	Ala	Ala	Arg	Ser	Asp			
325							330				335							
ctg	ctg	gtt	gat	cag	tgg	aag	aag	gcc	gag	ctg	tat	cgc	aca	aac			1056	

Leu	Leu	Val	Asp	Gln	Trp	Lys	Lys	Ala	Glu	Leu	Tyr	Arg	Thr	Asn				
															340	345	350	
gtg	ctg	ctg	att	ccg	ttg	ggt	gac	gac	ttc	cgc	ttc	aag	cag	aac	acc		1104	
Val	Leu	Ile	Pro	Leu	Gly	Asp	Asp	Phe	Arg	Phe	Lys	Gln	Asn	Thr				
															355	360	365	
gag	tgg	gat	gtg	cag	cgc	gtg	aac	tac	gaa	agg	ctg	ttc	gaa	cac	atc		1152	
Glu	Trp	Asp	Val	Gln	Arg	Val	Asn	Tyr	Glu	Arg	Leu	Phe	Glu	His	Ile			
															370	375	380	
aac	agc	cag	gcc	cac	ttc	aat	gtc	cag	gcg	cag	ttc	ggc	aca	ctg	cag		1200	
Asn	Ser	Gln	Ala	His	Phe	Asn	Val	Gln	Ala	Gln	Phe	Gly	Thr	Leu	Gln			
															385	390	395	400
gaa	tac	ttt	gat	gca	gtg	cac	cag	gcg	gaa	agg	gcg	gga	caa	gcc	gag		1248	
Glu	Tyr	Phe	Asp	Ala	Val	His	Gln	Ala	Glu	Arg	Ala	Gly	Gln	Ala	Glu			
															405	410	415	
ttt	ccc	acg	cta	agc	ggt	gac	ttt	ttc	aca	tac	gcc	gat	cga	tcg	gat		1296	
Phe	Pro	Thr	Leu	Ser	Gly	Asp	Phe	Phe	Thr	Tyr	Ala	Asp	Arg	Ser	Asp			
															420	425	430	
aac	tat	tgg	agt	ggc	tac	tac	aca	tcc	cgc	ccg	tat	cat	aag	cgc	atg		1344	
Asn	Tyr	Trp	Ser	Gly	Tyr	Tyr	Thr	Ser	Arg	Pro	Tyr	His	Lys	Arg	Met			
															435	440	445	
gac	cgc	gtc	ctg	atg	cac	tat	gta	cgt	gca	gca	gaa	atg	ctt	tcc	gcc		1392	
Asp	Arg	Val	Leu	Met	His	Tyr	Val	Arg	Ala	Ala	Glu	Met	Leu	Ser	Ala			
															450	455	460	
tgg	cac	tcc	tgg	gac	ggt	atg	gcc	cgc	atc	gag	gaa	cgt	ctg	gag	cag		1440	
Trp	His	Ser	Trp	Asp	Gly	Met	Ala	Arg	Ile	Glu	Glu	Arg	Leu	Glu	Gln			
															465	470	475	480
gcc	cgc	agg	gag	ctg	tca	ttg	ttc	cag	cac	cac	gac	ggt	ata	act	ggc		1488	
Ala	Arg	Arg	Glu	Leu	Ser	Leu	Phe	Gln	His	His	Asp	Gly	Ile	Thr	Gly			
															485	490	495	
aca	gca	aaa	acg	cac	gta	gtc	gtc	gac	tac	gag	caa	cgc	atg	cag	gaa		1536	
Thr	Ala	Lys	Thr	His	Val	Val	Val	Asp	Tyr	Glu	Gln	Arg	Met	Gln	Glu			
															500	505	510	
gct	tta	aaa	gcc	tgt	caa	atg	gta	atg	caa	cag	tcg	gtc	tac	cga	ttg		1584	
Ala	Leu	Lys	Ala	Cys	Gln	Met	Val	Met	Gln	Gln	Ser	Val	Tyr	Arg	Leu			
															515	520	525	
ctg	aca	aag	ccc	tcc	atc	tac	agt	ccg	gac	ttc	agt	ttc	ycg	tac	ttt		1632	
Leu	Thr	Lys	Pro	Ser	Ile	Tyr	Ser	Pro	Asp	Phe	Ser	Phe	Xaa	Tyr	Phe			
															530	535	540	
acg	ctc	gac	gac	tcc	cgc	tgg	cca	gga	tct	ggt	gtg	gag	gac	agt	cga		1680	
Thr	Leu	Asp	Asp	Ser	Arg	Trp	Pro	Gly	Ser	Gly	Val	Glu	Asp	Ser	Arg			
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acc	acc	ata	ata	ctg	ggc	gag	gat	ata	ctg	ccc	tcc	aag	cat	gtg	gtg		1728	
Thr	Thr	Ile	Ile	Leu	Gly	Glu	Asp	Ile	Leu	Pro	Ser	Lys	His	Val	Val			
															565	570	575	
atg	cac	aac	acc	ctg	ccc	cac	tgg	cg	gag	cag	ctg	gtg	gac	ttt	tat		1776	

Met His Asn Thr Leu Pro His Trp Arg Glu Gln Leu Val Asp Phe Tyr			
580	585	590	
gta tcc agt ccg ttt gta agc gtt acc gac ttg gca aac aat ccg gtg			1824
Val Ser Ser Pro Phe Val Ser Val Thr Asp Leu Ala Asn Asn Pro Val			
595	600	605	
gag gct cag gtg tcc ccg gtg tgg agc tgg cac cac gac aca ctc aca			1872
Glu Ala Gln Val Ser Pro Val Trp Ser Trp His His Asp Thr Leu Thr			
610	615	620	
aag act atc cac cca caa ggc tcc acc acc aag tac cgc atc atc ttc			1920
Lys Thr Ile His Pro Gln Gly Ser Thr Thr Lys Tyr Arg Ile Ile Phe			
625	630	635	640
aag gct cgg gtg ccg ccc atg ggc ttg gcc acc tac gtt tta acc atc			1968
Lys Ala Arg Val Pro Pro Met Gly Leu Ala Thr Tyr Val Leu Thr Ile			
645	650	655	
tcc gat tcc aag cca gag cac acc tcg tat gca tcg aat ctc ttg ctc			2016
Ser Asp Ser Lys Pro Glu His Thr Ser Tyr Ala Ser Asn Leu Leu Leu			
660	665	670	
cgt aaa aac ccg act tcg tta cca ttg ggc caa tat ccg gag gat gtg			2064
Arg Lys Asn Pro Thr Ser Leu Pro Leu Gly Gln Tyr Pro Glu Asp Val			
675	680	685	
aag ttt ggc gat cct cga gag atc tca ttg cgg gtt ggt aac gga ccc			2112
Lys Phe Gly Asp Pro Arg Glu Ile Ser Leu Arg Val Gly Asn Gly Pro			
690	695	700	
acc ttg gcc ttt tcg gag cag ggt ctc ctt aag tcc att cag ctt act			2160
Thr Leu Ala Phe Ser Glu Gln Gly Leu Leu Lys Ser Ile Gln Leu Thr			
705	710	715	720
cag gat agc cca cat gta ccg gtg cac ttc aag ttc ctc aag tat ggc			2208
Gln Asp Ser Pro His Val Pro Val His Phe Lys Phe Leu Lys Tyr Gly			
725	730	735	
gtt cga tcg cat ggc gat aga tcc ggt gcc tat ctg ttc ctg ccc aat			2256
Val Arg Ser His Gly Asp Arg Ser Gly Ala Tyr Leu Phe Leu Pro Asn			
740	745	750	
gga cca gct tcg cca gtc gag ctt ggc cag cca gtg gtc ctg gtg act			2304
Gly Pro Ala Ser Pro Val Glu Leu Gly Gln Pro Val Val Leu Val Thr			
755	760	765	
aag ggc aaa ctg gag tcg tcc gtg agc gtg gga ctt ccg agc gtg gtg			2352
Lys Gly Lys Leu Glu Ser Ser Val Ser Val Gly Leu Pro Ser Val Val			
770	775	780	
cac cag acg ata atg cgc ggt ggt gca cct gag att cgc aat ctg gtg			2400
His Gln Thr Ile Met Arg Gly Gly Ala Pro Glu Ile Arg Asn Leu Val			
785	790	795	800
gat ata ggc tca ctg gac aac acg gag atc gtg atg cgc ttg gag acg			2448
Asp Ile Gly Ser Leu Asp Asn Thr Glu Ile Val Met Arg Leu Glu Thr			
805	810	815	
cat atc gac agc ggc gat atc ttc tac acg gat ctc aat gga ttg caa			2496

His Ile Asp Ser Gly Asp Ile Phe Tyr Thr Asp Leu Asn Gly Leu Gln			
820	825	830	
ttt atc aag agg cgg cgt ttg gac aaa tta cct ttg cag gcc aac tat		2544	
Phe Ile Lys Arg Arg Arg Leu Asp Lys Leu Pro Leu Gln Ala Asn Tyr			
835	840	845	
tat ccc ata cct tcg ggt atg ttc att gag gat gcc aat acg cga ctc		2592	
Tyr Pro Ile Pro Ser Gly Met Phe Glu Asp Ala Asn Thr Arg Leu			
850	855	860	
act ctc ctc acg ggt caa ccg ctg ggt gga tct tct ctg gcc tcg ggc		2640	
Thr Leu Leu Thr Gly Gln Pro Leu Gly Ser Ser Leu Ala Ser Gly			
865	870	875	880
gag cta gag att atg caa gat cgt cgc ctg gcc agc gat gat gaa cgc		2688	
Glu Leu Glu Ile Met Gln Asp Arg Arg Leu Ala Ser Asp Asp Glu Arg			
885	890	895	
ggc ctg gga cag ggt gtt ttg gac aac aag ccg gtg ctg cat att tat		2736	
Gly Leu Gly Gln Gly Val Leu Asp Asn Lys Pro Val Leu His Ile Tyr			
900	905	910	
cgg ctg gtg ctg gag aag gtt aac aac tgt gtc cga ccg tca aag ctt		2784	
Arg Leu Val Leu Glu Lys Val Asn Asn Cys Val Arg Pro Ser Lys Leu			
915	920	925	
cat cct gcc ggc tat ttg aca agt gcc gca cac aaa gca tcg cag tca		2832	
His Pro Ala Gly Tyr Leu Thr Ser Ala Ala His Lys Ala Ser Gln Ser			
930	935	940	
ctg ctg gat cca ctg gac aag ttt ata ttc gct gaa aat gag tgg atc		2880	
Leu Leu Asp Pro Leu Asp Lys Phe Ile Phe Ala Glu Asn Glu Trp Ile			
945	950	955	960
ggg gca cag ggg caa ttt ggt ggc gat cat cct tcg gct cgt gag gat		2928	
Gly Ala Gln Gly Gln Phe Gly Gly Asp His Pro Ser Ala Arg Glu Asp			
965	970	975	
ctc gat gtg tcg gtg atg aga cgc tta acc aag agc tcg gcc aaa acc		2976	
Leu Asp Val Ser Val Met Arg Arg Leu Thr Lys Ser Ser Ala Lys Thr			
980	985	990	
cag cga gta ggc tac gtt ctg cac cgc acc aat ctg atg caa tgc ggc		3024	
Gln Arg Val Gly Tyr Val Leu His Arg Thr Asn Leu Met Gln Cys Gly			
995	1000	1005	
act cca gag gag cat aca cag aag ctg gat gtg tgc cac cta ctg		3069	
Thr Pro Glu Glu His Thr Gln Lys Leu Asp Val Cys His Leu Leu			
1010	1015	1020	
ccg aat gtg gcg aga tgc gag gcg acg acg ctg act ttc ctg cag		3114	
Pro Asn Val Ala Arg Cys Glu Ala Thr Thr Leu Thr Phe Leu Gln			
1025	1030	1035	
aat ttg gag cac ttg gat ggc atg gtg gcg ccg gaa gtg tgc ccc		3159	
Asn Leu Glu His Leu Asp Gly Met Val Ala Pro Glu Val Cys Pro			
1040	1045	1050	
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Met Glu Thr Ala Ala Tyr Val Ser Ser His Ser Ser
1055 1060 1065

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Leu Gly Arg Ser Ser His His His His His Gly Glu Phe Asp Asp
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Pro Ile Arg Pro Pro Leu Lys Val Ala Arg Ser Pro Arg Pro Gly Gln
35 40 45

Cys Gln Asp Val Val Gln Asp Val Pro Asn Val Asp Val Gln Met Leu
50 55 60

Glu Leu Tyr Asp Arg Met Ser Phe Lys Asp Ile Asp Gly Gly Val Trp
65 70 75 80

Lys Gln Gly Trp Asn Ile Lys Tyr Asp Pro Leu Lys Tyr Asn Ala His
85 90 95

His Lys Leu Lys Val Phe Val Val Pro His Ser His Asn Asp Pro Gly
100 105 110

Trp Ile Gln Thr Phe Glu Glu Tyr Tyr Gln His Asp Thr Lys His Ile
115 120 125

Leu Ser Asn Ala Leu Arg His Leu His Asp Asn Pro Glu Met Lys Phe
130 135 140

Ile Trp Ala Glu Ile Ser Tyr Phe Ala Arg Phe Tyr His Asp Leu Gly
145 150 155 160

Glu Asn Lys Lys Leu Gln Met Lys Ser Ile Val Lys Asn Gly Gln Leu
165 170 175

Glu Leu Glu Phe Val Thr Gly Gly Trp Val Met Pro Asp Glu Ala Asn
180 185 190

Ser His Trp Arg Asn Val Leu Leu Gln Leu Thr Glu Gly Gln Thr Trp
195 200 205

Leu Lys Gln Phe Met Asn Val Thr Pro Thr Ala Ser Trp Ala Ile Asp
210 215 220

Pro Phe Gly His Ser Pro Thr Met Pro Tyr Ile Leu Gln Lys Ser Gly
225 230 235 240

Phe Lys Asn Met Leu Ile Gln Arg Thr His Tyr Ser Val Lys Lys Glu
245 250 255

Leu Ala Gln Gln Arg Gln Leu Glu Phe Leu Trp Arg Gln Ile Trp Asp
260 265 270

Asn Lys Gly Asp Thr Ala Leu Phe Thr His Met Met Pro Phe Tyr Ser
275 280 285

Tyr Asp Ile Pro His Thr Cys Gly Pro Asp Pro Lys Val Cys Cys Gln
290 295 300

Phe Asp Phe Lys Arg Met Gly Ser Phe Gly Leu Ser Cys Pro Trp Lys
305 310 315 320

Val Pro Pro Arg Thr Ile Ser Asp Gln Asn Val Ala Ala Arg Ser Asp
325 330 335

Leu Leu Val Asp Gln Trp Lys Lys Ala Glu Leu Tyr Arg Thr Asn
340 345 350

Val Leu Leu Ile Pro Leu Gly Asp Asp Phe Arg Phe Lys Gln Asn Thr
355 360 365

Glu Trp Asp Val Gln Arg Val Asn Tyr Glu Arg Leu Phe Glu His Ile
370 375 380

Asn Ser Gln Ala His Phe Asn Val Gln Ala Gln Phe Gly Thr Leu Gln
385 390 395 400

Glu Tyr Phe Asp Ala Val His Gln Ala Glu Arg Ala Gly Gln Ala Glu
405 410 415

Phe Pro Thr Leu Ser Gly Asp Phe Phe Thr Tyr Ala Asp Arg Ser Asp
420 425 430

Asn Tyr Trp Ser Gly Tyr Tyr Thr Ser Arg Pro Tyr His Lys Arg Met
435 440 445

Asp Arg Val Leu Met His Tyr Val Arg Ala Ala Glu Met Leu Ser Ala
450 455 460

Trp His Ser Trp Asp Gly Met Ala Arg Ile Glu Glu Arg Leu Glu Gln
465 470 475 480

Ala Arg Arg Glu Leu Ser Leu Phe Gln His His Asp Gly Ile Thr Gly
485 490 495

Thr Ala Lys Thr His Val Val Val Asp Tyr Glu Gln Arg Met Gln Glu
500 505 510

Ala Leu Lys Ala Cys Gln Met Val Met Gln Gln Ser Val Tyr Arg Leu
515 520 525

Leu Thr Lys Pro Ser Ile Tyr Ser Pro Asp Phe Ser Phe Xaa Tyr Phe
530 535 540

Thr Leu Asp Asp Ser Arg Trp Pro Gly Ser Gly Val Glu Asp Ser Arg
545 550 555 560

Thr Thr Ile Ile Leu Gly Glu Asp Ile Leu Pro Ser Lys His Val Val
565 570 575

Met His Asn Thr Leu Pro His Trp Arg Glu Gln Leu Val Asp Phe Tyr
580 585 590

Val Ser Ser Pro Phe Val Ser Val Thr Asp Leu Ala Asn Asn Pro Val
595 600 605

Glu Ala Gln Val Ser Pro Val Trp Ser Trp His His Asp Thr Leu Thr
610 615 620

Lys Thr Ile His Pro Gln Gly Ser Thr Thr Lys Tyr Arg Ile Ile Phe
625 630 635 640

Lys Ala Arg Val Pro Pro Met Gly Leu Ala Thr Tyr Val Leu Thr Ile
645 650 655

Ser Asp Ser Lys Pro Glu His Thr Ser Tyr Ala Ser Asn Leu Leu Leu
660 665 670

Arg Lys Asn Pro Thr Ser Leu Pro Leu Gly Gln Tyr Pro Glu Asp Val
675 680 685

Lys Phe Gly Asp Pro Arg Glu Ile Ser Leu Arg Val Gly Asn Gly Pro
690 695 700

Thr Leu Ala Phe Ser Glu Gln Gly Leu Leu Lys Ser Ile Gln Leu Thr
705 710 715 720

Gln Asp Ser Pro His Val Pro Val His Phe Lys Phe Leu Lys Tyr Gly
725 730 735

Val Arg Ser His Gly Asp Arg Ser Gly Ala Tyr Leu Phe Leu Pro Asn
740 745 750

Gly Pro Ala Ser Pro Val Glu Leu Gly Gln Pro Val Val Leu Val Thr
755 760 765

Lys Gly Lys Leu Glu Ser Ser Val Ser Val Gly Leu Pro Ser Val Val
770 775 780

His Gln Thr Ile Met Arg Gly Gly Ala Pro Glu Ile Arg Asn Leu Val
785 790 795 800

Asp Ile Gly Ser Leu Asp Asn Thr Glu Ile Val Met Arg Leu Glu Thr
805 810 815

His Ile Asp Ser Gly Asp Ile Phe Tyr Thr Asp Leu Asn Gly Leu Gln
820 825 830

Phe Ile Lys Arg Arg Arg Leu Asp Lys Leu Pro Leu Gln Ala Asn Tyr
835 840 845

Tyr Pro Ile Pro Ser Gly Met Phe Ile Glu Asp Ala Asn Thr Arg Leu
850 855 860

Thr Leu Leu Thr Gly Gln Pro Leu Gly Gly Ser Ser Leu Ala Ser Gly
865 870 875 880

Glu Leu Glu Ile Met Gln Asp Arg Arg Leu Ala Ser Asp Asp Glu Arg
885 890 895

Gly Leu Gly Gln Gly Val Leu Asp Asn Lys Pro Val Leu His Ile Tyr
900 905 910

Arg Leu Val Leu Glu Lys Val Asn Asn Cys Val Arg Pro Ser Lys Leu
915 920 925

His Pro Ala Gly Tyr Leu Thr Ser Ala Ala His Lys Ala Ser Gln Ser
930 935 940

Leu Leu Asp Pro Leu Asp Lys Phe Ile Phe Ala Glu Asn Glu Trp Ile
945 950 955 960

Gly Ala Gln Gly Gln Phe Gly Gly Asp His Pro Ser Ala Arg Glu Asp
965 970 975

Leu Asp Val Ser Val Met Arg Arg Leu Thr Lys Ser Ser Ala Lys Thr
980 985 990

Gln Arg Val Gly Tyr Val Leu His Arg Thr Asn Leu Met Gln Cys Gly
995 1000 1005

Thr Pro Glu Glu His Thr Gln Lys Leu Asp Val Cys His Leu Leu
1010 1015 1020

Pro Asn Val Ala Arg Cys Glu Ala Thr Thr Leu Thr Phe Leu Gln
1025 1030 1035

Asn Leu Glu His Leu Asp Gly Met Val Ala Pro Glu Val Cys Pro
1040 1045 1050

Met Glu Thr Ala Ala Tyr Val Ser Ser His Ser Ser
1055 1060 1065

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Arg Ser Ser His His His His His Gly Glu Phe Asp Asp Pro Ile
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Arg Pro Pro Leu Lys Val Ala Arg Ser Pro Arg Pro Gly Gln Cys Gln
20 25 30

Asp Val Val Asp Gln Val Pro Asn Val Asp Gln Met Leu Glu Leu Tyr
10

35

40

45

Asp Arg Met Ser Phe Lys Asp Ile Asp Gly Gly Val Trp Lys Gln Gly
50 55 60

Trp Asn Ile Lys Tyr Asp Pro Leu Lys Tyr Asn Ala His His Lys Leu
65 70 75 80

Lys Val Phe Val Val Pro His Ser His Asn Asp Pro Gly Trp Ile Gln
85 90 95

Thr Phe Glu Glu Tyr Tyr Gln His Asp Thr Lys His Ile Leu Ser Asn
100 105 110

Ala Leu Arg His Leu His Asp Asn Pro Glu Met Lys Phe Ile Trp Ala
115 120 125

Glu Ile Ser Tyr Phe Ala Arg Phe Tyr His Asp Leu Gly Glu Asn Lys
130 135 140

Lys Leu Gln Met Lys Ser Ile Val Lys Asn Gly Gln Leu Glu Phe Val
145 150 155 160

Thr Gly Gly Trp Val Met Pro Asp Glu Ala Asn Ser His Trp Arg Asn
165 170 175

Val Leu Leu Gln Leu Thr Glu Gly Gln Thr Trp Leu Lys Gln Phe Met
180 185 190

Asn Val Thr Pro Thr Ala Ser Trp Ile Asp Pro Phe Gly His Ser Pro
195 200 205

Thr Met Pro Tyr Ile Leu Gln Lys Ser Gly Phe Lys Asn Met Leu Ile
210 215 220

Gln Arg Thr His Tyr Ser Val Lys Lys Glu Leu Ala Gln Gln Arg Gln
225 230 235 240

Leu Glu Phe Leu Trp Arg Gln Ile Trp Asp Asn Lys Gly Asp Thr Ala
245 250 255

Leu Phe Thr His Met Met Pro Phe Tyr Ser Tyr Asp Ile Pro His Thr
260 265 270

Cys Gly Pro Asp Pro Lys Val Cys Cys Gln Phe Asp Phe Lys Arg Met

275

280

285

Gly Ser Phe Gly Leu Ser Cys Pro Trp Lys Val Pro Pro Arg Thr Ile
290 295 300

Ser Asp Gln Asn Val Ala Ala Arg Ser Asp Leu Leu Val Asp Gln Trp
305 310 315 320

Lys Lys Lys Ala Glu Leu Tyr Arg Thr Asn Val Leu Leu Ile Pro Leu
325 330 335

Gly Asp Asp Phe Arg Phe Lys Gln Asn Thr Glu Trp Asp Val Gln Arg
340 345 350

Val Asn Tyr Glu Arg Leu Phe Glu His Ile Asn Ser Gln Ala His Phe
355 360 365

Asn Val Gln Ala Gln Phe Gly Thr Gln Glu Tyr Phe Asp Ala Val His
370 375 380

Gln Ala Glu Arg Ala Gly Gln Ala Ala Glu Phe Pro Thr Leu Ser Gly
385 390 395 400

Asp Phe Phe Thr Tyr Ala Asp Arg Ser Asp Asn Tyr Trp Ser Gly Tyr
405 410 415

Tyr Thr Ser Arg Pro Tyr His Lys Arg Met Asp Arg Val Leu Met His
420 425 430

Tyr Val Arg Ala Ala Glu Met Leu Ser Ala Trp His Ser Trp Asp Gly
435 440 445

Met Ala Arg Ile Glu Glu Arg Leu Glu Gln Ala Arg Arg Glu Leu Ser
450 455 460

Leu Phe Gln His His Asp Gly Ile Thr Gly Thr Ala Lys Thr His Val
465 470 475 480

Val Val Asp Tyr Glu Gln Arg Met Gln Glu Ala Leu Lys Ala Cys Gln
485 490 495

Met Val Met Met Gln Gln Ser Val Tyr Arg Leu Leu Thr Lys Pro Ser
500 505 510

Ile Tyr Ser Pro Asp Phe Ser Phe Ser Tyr Phe Thr Leu Asp Asp Ser

515

520

525

Arg Trp Pro Gly Ser Gly Val Glu Asp Ser Arg Thr Thr Ile Ile Leu
530 535 540

Gly Glu Asp Ile Leu Pro Ser Lys His Val Val Met His Asn Thr Leu
545 550 555 560

Pro His Trp Arg Glu Gln Leu Val Asp Phe Tyr Val Ser Ser Pro Phe
565 570 575

Val Ser Val Thr Asp Leu Ala Asn Asn Pro Val Glu Ala Gln Val Ser
580 585 590

Pro Val Trp Ser Trp His His Asp Thr Leu Thr Lys Thr Ile His Pro
595 600 605

Gln Gly Ser Thr Thr Lys Tyr Arg Ile Ile Phe Lys Ala Arg Val Pro
610 615 620

Pro Met Gly Leu Ala Thr Tyr Val Leu Thr Ile Ser Lys Ser Lys Pro
625 630 635 640

Glu His Thr Ser Tyr Ala Ser Asn Leu Leu Leu Arg Lys Asn Pro Thr
645 650 655

Ser Leu Pro Leu Gly Gln Tyr Pro Glu Asp Val Lys Phe Gly Asp Pro
660 665 670

Arg Glu Ile Ser Leu Arg Val Gly Asn Gly Pro Thr Leu Ala Phe Ser
675 680 685

Glu Gln Gly Leu Leu Lys Ser Ile Gln Leu Thr Gln Asp Ser Pro His
690 695 700

Val Pro Val His Phe Lys Phe Leu Lys Tyr Gly Val Arg Ser His Gly
705 710 715 720

Asp Arg Ser Gly Ala Tyr Leu Phe Leu Pro Asn Gly Pro Ala Ser Pro
725 730 735

Val Glu Leu Gly Gln Pro Val Val Leu Val Thr Lys Gly Lys Leu Glu
740 745 750

Ser Ser Val Ser Val Gly Leu Pro Ser Val Val His Gln Thr Ile Met

755

760

765

Arg Gly Gly Ala Pro Glu Ile Arg Asn Leu Val Asp Ile Gly Ser Leu
770 775 780

Asp Asn Thr Glu Ile Val Met Arg Leu Glu Thr His Ile Asp Ser Gly
785 790 795 800

Asp Ile Phe Tyr Thr Asp Leu Asn Gly Leu Gln Phe Ile Lys Arg Arg
805 810 815

Arg Leu Asp Lys Leu Pro Leu Gln Ala Asn Tyr Tyr Pro Ile Pro Ser
820 825 830

Gly Met Phe Ile Glu Asp Ala Asn Thr Arg Leu Thr Leu Leu Thr Gly
835 840 845

Gln Pro Leu Gly Gly Ser Ser Leu Ala Ser Gly Glu Leu Glu Ile Met
850 855 860

Gln Asp Arg Arg Leu Ala Ser Asp Asp Glu Arg Gly Leu Gly Gln Gly
865 870 875 880

Val Leu Asp Asn Lys Pro Val Leu His Ile Tyr Arg Leu Val Leu Glu
885 890 895

Lys Val Asn Asn Cys Val Arg Pro Ser Lys Leu His Pro Ala Gly Tyr
900 905 910

Leu Thr Ser Ala Ala His Lys Ala Ser Gln Ser Leu Leu Asp Pro Leu
915 920 925

Asp Lys Phe Ile Phe Ala Glu Asn Glu Trp Ile Gly Ala Gln Gly Gln
930 935 940

Phe Gly Gly Asp His Pro Ser Ala Arg Glu Asp Leu Asp Val Ser Val
945 950 955 960

Met Arg Arg Leu Thr Lys Ser Ser Ala Lys Thr Gln Arg Val Gly Tyr
965 970 975

Val Leu His Arg Thr Asn Leu Met Gln Cys Gly Thr Pro Glu Glu His
980 985 990

Thr Gln Lys Leu Asp Val Cys His Leu Leu Pro Asn Val Ala Arg Cys

995

1000

1005

Glu Arg Thr Thr Leu Thr Phe Leu Gln Asn Leu Glu His Leu Asp
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Gly Met Val Ala Pro Glu Val Cys Pro Met Glu Thr Ala Ala Tyr
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Val Ser Ser His Ser Ser
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Val Val Glu Asp Gly Pro Lys Ser Ser Gln Ser Asn Phe Ser Gln Gly
35 40 45

Ala Gly Ser His Leu Leu Pro Ser Gln Leu Ser Ser Val Asp Thr Ala
50 55 60

Asp Cys Leu Phe Ala Ser Gln Ser Gly Ser His Asn Ser Asp Val Gln
65 70 75 80

Met Leu Asp Val Tyr Ser Leu Ile Ser Phe Asp Asn Pro Asp Gly Gly
85 90 95

Val Trp Lys Gln Gly Phe Asp Ile Thr Tyr Glu Ser Asn Glu Trp Asp
100 105 110

Thr Glu Pro Leu Gln Val Phe Val Val Pro His Ser His Asn Asp Pro
115 120 125

Gly Trp Leu Lys Thr Phe Asn Asp Tyr Phe Arg Asp Lys Thr Gln Tyr
130 135 140

Ile Phe Asn Asn Met Val Leu Lys Leu Lys Glu Asp Ser Arg Arg Lys
145 150 155 160

Phe Ile Trp Ser Glu Ile Ser Tyr Leu Ser Lys Trp Trp Asp Ile Ile
165 170 175

Asp Ile Gln Lys Lys Asp Ala Val Lys Ser Leu Glu Asn Gly Gln Leu
180 185 190

Glu Ile Val Thr Gly Gly Trp Val Met Pro Asp Glu Ala Thr Pro His
195 200 205

Tyr Phe Ala Leu Ile Asp Gln Leu Ile Glu Gly His Gln Glu Leu Glu
210 215 220

Asn Asn Ile Gly Val Lys Pro Arg Ser Gly Trp Ala Ile Asp Pro Phe
225 230 235 240

Gly His Ser Pro Thr Met Ala Tyr Leu Leu Asn Arg Ala Gly Leu Ser
245 250 255

His Met Leu Ile Gln Arg Val His Tyr Ala Val Lys Lys His Phe Ala
260 265 270

Leu His Lys Thr Leu Glu Phe Phe Trp Arg Gln Asn Trp Asp Leu Gly
275 280 285

Ser Val Thr Asp Ile Leu Cys His Met Met Pro Phe Tyr Ser Tyr Asp
290 295 300

Ile Pro Gly His Cys Gly Pro Asp Pro Lys Ile Cys Cys Gln Phe Asp
305 310 315 320

Phe Lys Arg Leu Pro Gly Gly Arg Phe Gly Cys Pro Gln Gly Val Pro
325 330 335

Pro Glu Thr Ile His Pro Gly Asn Val Gln Ser Arg Ala Arg Met Leu
340 345 350

Leu Asp Gln Tyr Arg Lys Lys Ser Lys Leu Phe Arg Thr Lys Val Leu
355 360 365

Leu Ala Pro Leu Gly Asp Asp Phe Arg Tyr Cys Glu Tyr Thr Glu Trp
370 375 380

Asp Leu Gln Phe Lys Asn Tyr Gln Gln Leu Phe Asp Tyr Met Asn Ser
385 390 395 400

Gln Ser Lys Phe Lys Val Lys Ile Gln Phe Gly Thr Leu Ser Asp Phe
405 410 415

Phe Asp Ala Leu Asp Lys Ala Asp Glu Thr Gln Arg Asp Lys Ser Gly
420 425 430

Gln Ser Met Phe Pro Val Leu Ser Gly Asp Phe Phe Thr Tyr Ala Asp
435 440 445

Arg Asp Asp His Tyr Trp Ser Gly Tyr Phe Thr Ser Arg Pro Phe Tyr
450 455 460

Arg Lys Met Arg Asp Arg Ile Met Glu Ser His Leu Arg Ala Ala Glu
465 470 475 480

Ile Leu Tyr Tyr Phe Ala Leu Arg Gln Ala His Lys Tyr Lys Ile Asn
485 490 495

Lys Phe Leu Ser Ser Leu Tyr Thr Ala Leu Thr Glu Arg Ala Arg
500 505 510

Asn Leu Gly Leu Phe Gln His His Asp Ala Ile Thr Gly Thr Ala Lys
515 520 525

Asp Trp Val Val Asp Tyr Gly Thr Arg Leu Phe His Ser Leu Met
530 535 540

Val Leu Glu Lys Ile Ile Gly Asn Ser Ala Phe Leu Leu Ile Gly Lys
545 550 555 560

Asp Lys Leu Thr Tyr Asp Ser Tyr Ser Pro Asp Thr Phe Leu Glu Met
565 570 575

Asp Leu Lys Gln Lys Ser Gln Asp Ser Leu Pro Gln Lys Asn Ile Ile
580 585 590

Arg Leu Ser Ala Glu Pro Arg Tyr Leu Val Val Tyr Asn Asn Pro Leu
595 600 605

Glu Gln Asp Arg Ile Ser Leu Val Ser Val Tyr Val Ser Ser Pro Thr
610 615 620

Val Gln Val Phe Ser Ala Ser Gly Lys Pro Val Glu Val Gln Val Ser
625 630 635 640

Ala Val Trp Asp Thr Ala Asn Thr Ile Ser Glu Thr Ala Tyr Glu Ile
645 650 655

Ser Phe Arg Ala His Ile Pro Pro Leu Gly Leu Lys Val Tyr Lys Ile
660 665 670

Leu Glu Ser Ala Ser Ser Asn Ser His Leu Ala Asp Tyr Val Leu Tyr
675 680 685

Lys Asn Lys Val Glu Asp Ser Gly Ile Phe Thr Ile Lys Asn Met Ile
690 695 700

Asn Thr Glu Glu Gly Ile Thr Leu Glu Asn Ser Phe Val Leu Leu Arg
705 710 715 720

Phe Asp Gln Thr Gly Leu Met Lys Gln Met Met Thr Lys Glu Asp Gly
725 730 735

Lys His His Glu Val Asn Val Gln Phe Ser Trp Tyr Gly Thr Thr Ile
740 745 750

Lys Arg Asp Lys Ser Gly Ala Tyr Leu Phe Leu Pro Asp Gly Asn Ala
755 760 765

Lys Pro Tyr Val Tyr Thr Thr Pro Pro Phe Val Arg Val Thr His Gly
770 775 780

Arg Ile Tyr Ser Glu Val Thr Cys Phe Phe Asp His Val Thr His Arg
785 790 795 800

Val Arg Leu Tyr His Ile Gln Gly Ile Glu Gly Gln Ser Val Glu Val
805 810 815

Ser Asn Ile Val Asp Ile Arg Lys Val Tyr Asn Arg Glu Ile Ala Met
820 825 830

Lys Ile Ser Ser Asp Ile Lys Ser Gln Asn Arg Phe Tyr Thr Asp Leu
835 840 845

Asn Gly Tyr Gln Ile Gln Pro Arg Met Thr Leu Ser Lys Leu Pro Leu
850 855 860

Gln Ala Asn Val Tyr Pro Met Thr Thr Met Ala Tyr Ile Gln Asp Ala
865 870 875 880

Lys His Arg Leu Thr Leu Leu Ser Ala Gln Ser Leu Gly Val Ser Ser
885 890 895

Leu Asn Ser Gly Gln Ile Glu Val Ile Met Asp Arg Arg Leu Met Gln
900 905 910

Asp Asp Asn Arg Gly Leu Glu Gln Gly Ile Gln Asp Asn Lys Ile Thr
915 920 925

Ala Asn Leu Phe Arg Ile Leu Leu Glu Lys Arg Ser Ala Val Asn Thr
930 935 940

Glu Glu Glu Lys Lys Ser Val Ser Tyr Pro Ser Leu Leu Ser His Ile
945 950 955 960

Thr Ser Ser Leu Met Asn His Pro Val Ile Pro Met Ala Asn Lys Phe
965 970 975

Ser Ser Pro Thr Leu Glu Leu Gln Gly Glu Phe Ser Pro Leu Gln Ser
980 985 990

Ser Leu Pro Cys Asp Ile His Leu Val Asn Leu Arg Thr Ile Gln Ser
995 1000 1005

Lys Val Gly Asn Gly His Ser Asn Glu Ala Ala Leu Ile Leu His
1010 1015 1020

Arg Lys Gly Phe Asp Cys Arg Phe Ser Ser Lys Gly Thr Gly Leu
1025 1030 1035

Phe Cys Ser Thr Thr Gln Gly Lys Ile Leu Val Gln Lys Leu Leu
1040 1045 1050

Asn Lys Phe Ile Val Glu Ser Leu Thr Pro Ser Ser Leu Ser Leu
1055 1060 1065

Met His Ser Pro Pro Gly Thr Gln Asn Ile Ser Glu Ile Asn Leu
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Ser Pro Met Glu Ile Ser Thr Phe Arg Ile Gln Leu Arg
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Asp Pro Lys Xaa Cys Cys Gln Phe Asp Phe Lys Arg
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Leu Leu Xaa Pro Leu Gly Asp Asp Phe Arg
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